## REMARKS

Entry of this amendment and allowance are requested.

The pending claims remain claims 1-27.

It is proposed to amend claim 1 to specifically recite what is implicit in the prior language of the claim, *i.e.*, it is the mixture of target oligonucleotide and impurity that is bound to the titratable anion exchange composition. The amendments to claim 1 do not raise any new issues as the added language as noted, is implicit in the prior language of claim 1. Furthermore, there is prior reference to the mixture of target oligonucleotide and impurity in claim 24. Accordingly, entry of the proposed amendments to claim 1 is requested although the Applicant considers all of the pending claims to be allowable with or without the proposed amendments to claim 1.

The Examiner is requested to reconsider the Section 102(b) rejection of claims 1-8, 10, 12, 14, 16, 18, 19, 24 and 25 as anticipated by Bambara *et al.* With respect, it is submitted that the Applicant's invention as defined in the rejected claims is not disclosed by Bambara *et al.*

Manifestly, to constitute an anticipation of claims, a reference must show, expressly or inherently, all of the features of the claims. Bambara *et al.* does not meet this test with respect to the Applicant's rejected claims.

More specifically, claim 1 (and all of the Applicant's other claims by virtue of their dependency) require the use of two steps. The first step is binding said target oligonucleotide to said titratable anion exchange composition in the presence of a solution having a first pH. The second step comprises passing a solution through the titratable anion exchange composition with target oligonucleotide bound thereon, wherein the pH of the solution is increased over time to a pH higher than said first pH thereby to elute the target oligonucleotide and wherein the impurity elutes at a different pH than the target oligonucleotide. This is in marked contrast to what Bambara *et al.* discloses. Thus, Bambara *et al.* loads its sample onto the solid support with a solution of pH 8.5. This is the step in Bambara *et al.* that corresponds to the first step of the Applicant's claims. The Examiner will note that, if the oligonucleotide does not "bind" to the column, it will simply pass straight through. Therefore, the pH of the "first solution" disclosed by Bambara *et al.* is 8.5. Bambara *et al.* then passes a second solution of pH 7.5 which causes the urea impurity to elute. This solution or step is manifestly NOT the equivalent to the first step of the present claims.

The Applicant notes the Examiner's comment in the second paragraph on page 4 of the action, where the Examiner states that "after loading the sample, Bambara *et al.* lower the pH. . ." However Bambara's solution with pH 7.5 is clearly not the solution present when the oligonucleotide is loaded on the support. The oligonucleotide has already been loaded onto the support when this solution is introduced.

Finally, Bambara *et al.* discloses eluting the oligonucleotide using a solution having a pH of 8.5. This is the step in Bambara that corresponds to the second step of the present claims. However, the pH of the second solution in Bambara *et al.* is exactly the same as the pH of the first solution employed to load the oligonucleotide onto the solid support. Bambara *et al.*, therefore, does not disclose a process where the pH is increased over time to a pH higher than that of the first solution employed to load the oligonucleotide onto the support as the Applicant's claims require. Bambara *et al.* therefore does not disclose a process having each and every feature of the present claims

In the circumstances, the Applicant respectfully submits that the rejected claims clearly and unequivocally define subject matter which is novel over Bambara *et al.* Accordingly, the Applicant submits that the Section 102(b) rejection should be withdrawn.

In connection with the foregoing, the Applicant has noted the Examiner's comment (second paragraph, page 4 of the action) that the binding of the target oligonucleotide at the lower pH and its solution at a higher pH are properties of the target oligonucleotide, so that the method of Bambara *et al.* and the claimed invention rely on these same properties. However, this conclusion is simply not borne out by the disclosure of Bambara *et al.* Bambara *et al.* uses the same pH to both load and elute the oligonucleotide. Bambara *et al.* is therefore clearly not relying upon the same properties as the method of the present invention.

The Examiner is also requested to reconsider and withdraw the Section 103(a) rejections of claims 13 and 17; claims 4, 8 and 15; claims 8 and 11; claim 9; claims 20-23 and 26; and claims 27 as set out in paragraphs 4-9, pages 5-6 of the action.

These rejections are based primarily on Bambara *et al.* which fails to disclose or suggest the Applicant's invention for the reasons noted above. The secondary references relied on by the Examiner do not fill in the substantive deficiencies of Bambara *et al.* and it would not, in any sense be obvious to one of ordinary skill to

modify the disclosure of Bambara *et al.* to produce a process according to the present claims, either in view of Bambara *et al.* alone, or in combination with any of the Examiner's other cited references. There is clearly no teaching that would cause one of ordinary skill in the art to contemplate the method of the present invention. For instance, in the case of separating a target oligonucleotide from other oligonucleotides (as, for instance, claimed in Applicant's claim 17), Bambara *et al.* goes to great lengths to avoid the use of an increasing pH gradient to separate target oligonucleotides, including using physical removal bands of purified material from chromatography plates. This goes contrary to the Applicant's invention and underscores its unobviousness.

In view of the foregoing, the Applicant submits that the claims herein should be found allowable. Such action is respectfully requested.

Respectfully submitted,

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